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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/973,105	10/09/2001	Jeffrey H. Baxter	6815.US.01	5606

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EXAMINER	
GHALI, ISIS A D	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/973,105	BAXTER, JEFFREY H.	
	Examiner	Art Unit	
	Isis A. Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicant's amendment filed 03/20/2007.

Claims 2, and 7-43 have been canceled.

Claims 1, 3-6 are pending and included in the prosecution.

The following rejection has been overcome by virtue of applicant's amendment and remarks:

The rejection of claims 1, 3 and 4 under 35 U.S.C. 102(b) as being anticipated by EP '462.

The following rejections are previously discussed in the office action dated 07/25/2006, and are maintained for reasons of record:

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 3-6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 10/266,317. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the copending application are directed to method for providing glutamine supplementation to a human comprising oral administration of N-acetyl-L-glutamine. The difference between the present claims and the claims of the copending application is that the present claims are directed to liquid composition and the claims of the copending application are not reciting any specific form of the composition. Therefore, the liquid composition of the present claims anticipates the composition of the claims of the copending application that encompasses liquid as well as any other compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

3. Applicant's arguments filed 03/20/2007 have been fully considered but they are not persuasive. Applicant submitting that:

"Responsive to this rejection, submitted herewith is a Terminal Disclaimer under 37 CFR 1.321(b) that specifies that the term of any patent issuing from this application shall not extend beyond the term of any patents issuing from the referenced copending application."

However, no terminal disclaimer has been filed, therefore, the rejection is maintained.

Specification

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Applicant has not respond to the objection made to the specification, nor indicated review for possible errors, therefore the objection is maintained.

The following new ground of rejections are necessitated by applicant's amendment:

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, and 3-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 27 and 28 are amended to recite the formula "contains no free glutamine", and this amendment introduced new matter that is not described in the original specification as of the filing date. Nowhere applicants have disclosed formula free from free glutamine. To the contrary, in page 6, lines 5-17, applicants disclosed nutritional formula as follows:

> "i. Free glutamine at 1.1 grams/liter, as determined by methods well known to one skilled in the art.
> ii. A blend of intact and lightly hydrolyzed proteins containing 50.0 grams /liter protein,.
> iii. N-Acetyl-L-glutamine at 11.6 grams/liter, which contains 9.0 grams of glutamine."

Further applicants disclosed in page 6, lines 18-20:

> "Total Glutamine is therefore the sum of these three sources, as: 1.1 grams/L (free) + (3.4 g/100 g protein x 50 g protein/L) + 9.0 grams/L (NAQ) = 11.8 grams."

In page 13, line 28 till page 14 line 3, applicants disclosed:

> "The amount of N-acetyl-L-glutamine or a nutritionally acceptable salt thereof utilized in a liquid nutritional formula will be dependent upon various factors including whether the formula provides a majority or sole source of nutrition, whether the formula contains other sources of glutamine, the amount of formula consumed on a daily basis, and the type of patient for whom the formula is intended (which will also influence the amount of formula consumed daily). The formula will preferably contain N-acetyl-L-glutamine or a nutritionally acceptable salt thereof in an amount sufficient, when combined with the glutamine contained in the other protein components, to provide at least 140 mg of total glutamine per kg of body weight per day."

Accordingly, no disclosure of formula contains no free glutamine, however, applicants disclosed free glutamine as part of the total glutamine content when applicants calculate the concentration of glutamine in the disclosed formula.

In accordance to MPEP 714.02, applicant should specifically point out to where in the disclosure a support for any amendment made to the claims can be found.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 3, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 540 462 ('462) in view of Bergana et al.

EP '462 teaches liquid nutritional formulation comprising N-acetyl-L-glutamine salts (abstract; page 2, lines 42-44, 55-58; page 3, lines 57-58). The amount of

glutamine given ranges from 0.1 to 70 g/kg/day (page 3, lines 9-15), and this amount is calculated to be equal to 0.532 to 37.24 mmol/kg/day, i.e. applicant' claimed amounts fall within the disclosure of the reference. The reference further disclosed that the formulation could contain only L-glutamine as the source of glutamine (page 5, claims 5 and 8). When glutamine added to drink, it does not inhibit gastric emptying to a physiological significant degree, and accordingly secures maximum fluid and nutrient availability (page 2, lines 49-50). The composition is essential for the treatment of fall in blood L-glutamine level (abstract)

Although EP '462 recognized oral formulation comprising glutamine wherein the glutamine is acetylated glutamine because it is more stable, however, applicants may argue that the reference does not teach formulation free of free glutamine.

Bergana et al. teach and realize the problem of unstability of glutamine fortified formula in aqueous solution, and found solution for the problem and established stability by replacing free glutamine by N-acetyl-L-glutamine that provided less metabolites (page 6003, 6009).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a oral formula comprising nutrient solution comprising acetylated glutamine and use N-acetyl-L-glutamine as the only source of glutamine in the formula because formula containing N-acetyl-L-glutamine is taught by Bergana et al. to be more stable in aqueous solution than formula containing free glutamine, with reasonable expectation of having storage stable nutritional solution

comprising N-acetyl-L-glutamine, and other nutrient, wherein the N-acetyl-L-glutamine is the only source of glutamine in the formula.

Response to Arguments

9. Applicant's arguments filed 03/20/2007 have been fully considered but they are not persuasive.

Although applicants acknowledge that the reference teaches either peptide form of glutamine or N-acetylated glutamine, however, applicants argue that the reference fails to specifically disclose any composition that actually contains N-acetyl-L-glutamine. The reference failed to disclose liquid composition comprising N-acetyl-L-glutamine that is unstable in liquids.

In response to this argument, applicant attention is drawn to the expression "comprising" of claim 1 that recites "glutamine supplementation comprising". The claim's language does not exclude the presence of peptide forms of glutamine and free glutamine.

Regarding the argument that the reference fails to show liquid composition comprising N-acetyl-L- glutamine, it is argued that in considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). EP '462 suggested liquid formulation, and suggested acetylated glutamine salts as they are more stable than glutamine, as admitted by applicant. The rational to modify or to combine the prior art does not have to be expressly stated in the

prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

In any event, the new ground of rejection teaches the invention as a whole.

A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

10. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of EP '462 and Bergana et al., and further in view of US 3,178,342 ('342).

The combined teachings of EP '462 and Bergana et al. are discussed above.

Although EP '462 realized that acetylated glutamine salts are more stable than glutamine, however, the combination of the references does not explicitly teach the specific salts of glutamine as claimed in claim 5.

US '342 teaches dimethyl ethanol amine salt of acetyl glutamine given orally and has remarkable effect on motor system and psychic development of the human being without affecting the autonomous nervous system (col.1, lines 1-18, 46-50; col.2, lines 66-67; 71; col.3, lines 1-4; claims 1-3).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a composition comprising nutrient solution comprising N-acetyl-glutamine salt and use N-acetyl-L-glutamine as the only source of glutamine in the formula as taught by the combination of EP '462 and Bergana et al., and select the dimethyl ethanol amine salt of acetyl glutamine disclosed by US '342, motivated by the teaching of US '342 that dimethyl ethanol amine salt of acetyl glutamine given has remarkable effect on motor system and psychic development of the human being without affecting the autonomous nervous system, with reasonable expectation of having solution comprising dimethyl ethanol amine salt of acetyl glutamine as the only source of glutamine that while providing nutrients to the human being will simultaneously provide remarkable effect on motor system and psychic development without affecting the autonomous nervous system.

Response to Arguments

11. Applicant's arguments filed 03/20/2007 have been fully considered but they are not persuasive.

Applicant hereby repeats the argument regarding EP '462. Applicant argues that none of EP '462 or US '342 actually teach formulation comprising N-acetyl-L-glutamine. Applicant argues that even references were combined, one would not have expected that the new formulation would result in composition more effective in many respects as glutamine source than composition containing free glutamine. Applicant argues that a study was conducted that suggests that N-acetyl-L-glutamine has a positive effect on the cells of the small intestine, even beyond that of glutamine. Additionally, electron transmission micrographs of enterocyte cytoplasm from healthy and malnourished pigs shown in Figures 7 and 8 of Applicants' Specification show that N-acetyl-L-glutamine is more effective than glutamine at preventing the overt signs of inflammation in the epithelial lining of the gastrointestinal tract.

In response to this argument, the examiner hereby repeats the response with regard to EP '462 as in section 9 of this office action. Further, it is argued that EP '462 suggested acetylated glutamine salts and US '342 teaches specific salt claimed by applicant "dimethyl ethanol amine salt of acetyl glutamine". Further, US '342 teaches oral drinkable solution, claim 1 of the reference. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to use dimethyl ethanol amine salt of acetyl glutamine disclosed by US '342, motivated by the teaching of US '342 that dimethyl ethanol amine

salt of acetyl glutamine given has remarkable effect on motor system and psychic development of the human being without affecting the autonomous nervous system, with reasonable expectation of having solution comprising dimethyl ethanol amine salt of acetyl glutamine.

A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

Regarding applicants' study, the presented data and study are moot in view of the new rejection over the combined teaching of EP '342 and Bergana et al. because the combination teaches composition comprising N-acetyl-L-glutamine and no free glutamine. Additionally, figure 7, as no figure 8 in the application as indicated by applicant, shows that N-acetyl-L-glutamine is more effective than glutamine at preventing the overt signs of inflammation in the epithelial lining of the gastrointestinal tract, and does not show the effect of formulation free of free glutamine versus formulation comprising both.

12. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of EP '462 and Bergana et al., and further in view Klimberg et al.

The combined teachings of EP '462 and Bergana et al. are discussed above. However, the combination of EP '462 and Bergana et al. does not teach the conditions that human being could be suffering and therefore given the glutamine containing supplement.

Klimberg teaches that oral glutamine accelerates healing of the small intestine and it is essential dietary component for the gut mucosa (page 1040, left column; page 1042, right column).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a composition comprising nutrient solution comprising N-acetyl-glutamine salt as disclosed by EP '462, and use the nutrient solution in patient with gut deterioration as disclosed by Klimberg et al., motivated by the teaching of Klimberg et al. that oral glutamine accelerates healing of the small intestine and it is essential dietary component for the gut mucosa, with reasonable expectation of having nutrient solution comprising N-acetyl-glutamine salt used to accelerate healing of compromised small intestine from any disease or particular treatment.

Response to Arguments

13. Applicant's arguments filed 03/20/2007 have been fully considered but they are not persuasive.

Applicant hereby repeats the argument regarding EP '462. applicant further argues that Klimberg does not teach N-acetyl-L-glutamine. None of EP '462 and Klimberg suggests nutritional formula actually contains N-acetyl-L-glutamine.

In response to applicant's argument against EP '462, the examiner hereby repeats the response as in section 9 of this office action. It is further argued that Klimberg is relied upon for the solely teaching of that the use of oral glutamine to accelerate healing of the small intestine and it is essential dietary component for the gut mucosa. One having ordinary skill in the art will have used N-acetyl-L- glutamine to accelerate healing of the small intestine because it is disclosed by EP '462 combined with Bergana that N-acetyl-L- glutamine is stable.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis A Ghali
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